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**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/440,829 | Applicant(s) CHENCHIK ET AL. | |
|---|---|---|---|
| | Examiner BJ Forman | Art Unit 1655 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 May 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3 and 7-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 7-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

**DETAILED ACTION**

1. This action is in response to papers filed 29 May 2001 in Paper No. 12 in which claims 1, 3, 10-14 and 16-23 were amended and claims36-38 were added and Paper No. 13 is which a Terminal Disclaimer was filed to overcome the obviousness type double patenting rejection of copending Application No. 09/417,268. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 8 dated 29 December 2000 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed bur are deemed moot in view of the amendments and withdrawn rejections. New grounds for rejection are discussed.

Currently claims 1-3, 7-23, 35 and 36-38 are under prosecution.

***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: which define or describe "hybridization efficiency"; which define of describe determining "variance in hybridization efficiency"; and which define or describe the probe elements that are measured to determine 10-fold variance. It is suggested that the claims be amended to recite the missing elements defining or describing "hybridization efficiency", "variance in hybridization efficiency" and "10-fold" "variance".

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3 & 10-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998) in view of Bresser et al. (U.S. Patent No. 5,707,801, issued 13 January 1998).

Regarding Claim 1, Brown et al. disclose an array (i.e. a multi-cell substrate) comprising at least one pattern of probe oligonucleotide spots (i.e. cells of the multi-cell substrate, each cell comprising a microarray; Column 11, lines 52-67) wherein the probe spots are stably associated with the surface of a solid support (Column 4, lines 35-44), wherein each probe spot corresponds to a target nucleic acid and comprises a composition of probes of at least 50 nucleotides (Column 13, lines 21-25) but they do not teach the probes range in length from about 50 to 120 nucleotides. However, probes of about 50 to 120 nucleotides were well known in the art at the time the claimed invention was made as taught by Bresser et al. who specifically teach that probes ranging in length from about 50 to 120 nucleotides provide for the most sensitive, rapid and stable hybridization (Column 9, lines 50-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of at least 50 nucleotides taught by Brown et al. with the teaching of Bresser et al. wherein the preferred probes are about 50 to 120 nucleotides for the benefits sensitive, rapid and stable hybridization as taught by Bresser et al. (Column 9, lines 50-58).

Regarding Claim 2, Brown et al. disclose the array (multi-cell substrate) wherein two or more different target nucleic acids are represented in said pattern (Column 4, lines 52-55).

Regarding Claim 3, Brown et al. disclose the array (multi-cell substrate) wherein each oligonucleotide spot (microarray) corresponds to a different target nucleic acid i.e. different target yeast nucleic acids are arrayed in different spots (cells) of the array (Example 3, Column 18, lines 39-43).

Regarding Claim 10, Brown et al. disclose the array (multi-cell substrate) wherein the density of spots (cells) on said array does not exceed about 1000/$cm^2$ (Column 11, lines 62-67).

Regarding Claim 11, Brown et al. disclose the array (multi-cell substrate) wherein the density of spots (cells) on said array does not exceed about 400/$cm^2$ (Column 11, lines 62-67).

Regarding Claim 12, Brown et al. disclose the array (multi-cell substrate) wherein the number of spots (cells) on said array ranges from about 50 to 10,000 i.e. 96 (Column 11, lines 62-67).

Regarding Claim 13, Brown et al. disclose the array (multi-cell substrate) wherein the number of spots (cells) on said array ranges from about 50 to 1,000 i.e. 96 (Column 11, lines 62-67).

Regarding Claim 14, Brown et al. teach an array (i.e. a multi-cell substrate) comprising a pattern of probe oligonucleotide spots (i.e. cells of the multi-cell substrate) (Column 11, lines 52-67) wherein the probe spots are bound to the surface of a solid support, wherein each probe spot corresponds to a target nucleic acid and comprises a composition of probes wherein the probe have a length of at least 50 nucleotides (Column 13, lines 21-25) but they do not specifically teach the probes range in length from about 60 to 100 nucleotides. However, probes of about 60 to 100 nucleotides were well known in the art at the time the claimed invention was made a taught by Bresser et al. who specifically teach that probes ranging in length from about 60 to 100 nucleotides provide the most sensitive, rapid and stable hybrids (Column 9, lines 50-58). It would have been obvious to one of ordinary skill in the art at the

time the claimed invention was made to modify the probes of at least 50 nucleotides taught by Brown et al. with the teaching of Bresser et al. wherein the preferred probes are about 50 to 120 nucleotides for the benefits sensitive, rapid and stable hybridization as taught by Bresser et al. (Column 9, lines 50-58).

Regarding Claim 15, Brown et al. teach the array wherein a ten or more different target nucleic acids are represented in said patterns i.e. 24 clones (Example 2, Columns 17-18)

Regarding Claim 16, Brown et al. teach the array wherein each oligonucleotide spot (cell) corresponds to a different target nucleic acid i.e. different target yeast nucleic acids are arrayed in different spots (cells) of the array (Example 3, Column 18, lines 39-43).

Regarding Claim 17, Brown et al. teach the array wherein two or more oligonucleotide spots correspond to the same target nucleic acid (Column 13, lines 4-10).

Regarding Claim 18, Brown et al. teach the array wherein the length of each of said unique oligonucleotides ranges from about 65 to 90 nucleotides i.e. at least 50 base pairs (Column 13, lines 21-22).

Regarding Claim 19, Brown et al. teach the array wherein the density of spots on said array does not exceed about 1000/$cm^2$ (Column 11, lines 62-67).

Regarding Claim 20, Brown et al. teach the array wherein the density of spots on said array does not exceed about 400/$cm^2$ (Column 11, 62-67).

Regarding Claim 21, Brown et al. teach the array wherein the number of spots on said array ranges from about 50 to 50,000 i.e. 96 (Column 11, 62-67).

Regarding Claim 22, Brown et al. teach the array wherein the number of spots on said array ranges from about 50 to 10,000 i.e. 96 (Column 11, 62-67).

**Response to Arguments**

6. Applicant argues that because Brown et al. probes greater than 50 nucleotides but does not teach an upper range of probe length, the length range teaching of Brown et al. at best overlaps with the claimed range of 50 to 120 nucleotides. The argument is deemed moot in view of the withdrawn rejection and new grounds for rejection. However, as the argument applies to the instant rejection, Brown et al. clearly teach a preferred probe length i.e. greater

than 50 nucleotides (Column 13, lines 21-24) and their preferred length overlaps the claimed range of 50 to 120. Additionally, Bresser et al. specifically teach probes of about 50 to 120 nucleotides wherein probes of this preferred length provides the most sensitive, rapid and stable hybridization (Column 9, lines 50-54). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the preferred probe length teaching of Bresser et al. to the preferred probes of Brown et al. for the expected benefit of providing the most sensitive, rapid and stable hybridization (Column 9, lines 50-54). Furthermore, it is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe length teachings of Brown et al. and Bresser et al. using routine experimentation to obtain the claimed probes for the obvious benefits of optimizing experimental conditions to thereby maximize hybridization results.

Applicant points to Example 6 of the specification to provide evidence of unexpected results. The argument is not found persuasive because Example 6 describes probes greater than 50 nucleotides (page 44, lines 1-3) which are described by Brown et al.. While Figure 1 illustrates the results of probes 50 to 100 nucleotides, Figure 1 and Example 6 do not describe or illustrate the results for probes less than 50 nucleotides or greater than 100 nucleotides for comparisons. Without a comparison to probes greater than 50 or less than 100 nucleotides, a showing of unexpected results is not demonstrated. Therefore Example 6 and Figure 1 do not demonstrate unexpected results for the claimed probes.

7. Claims 7 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998) and Bresser et al. (U.S. Patent No. 5,707,801, issued 13 January 1998) as applied to Claim 1 above and further in view of Chetverin et al. (WO 93/17126, 2 September 1993).

Regarding Claim 7, Brown et al. teach the array (i.e. a multi-cell substrate) comprising at least one pattern of probe oligonucleotide spots (i.e. cells of the multi-cell substrate each cell comprising a microarray; Column 11, lines 52-67) wherein the probe spots are stably associated with the surface of a solid support (Column 4, lines 35-44), wherein each probe spot

corresponds to a target nucleic acid and comprises a composition of probes wherein the probes are at least 50 nucleotides in length (Column 13, lines 21-25) but they do not specifically teach the probes range in length from about 50 to 120 nucleotides. However, probes of about 50 to 120 nucleotides were well known in the art at the time the claimed invention was made a taught by Bresser et al. who specifically teach that probes ranging in length from about 50 to 120 nucleotides provide the most sensitive, rapid and stable hybrids (Column 9, lines 50-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of at least 50 nucleotides taught by Brown et al. with the teaching of Bresser et al. wherein the preferred probes are about 60 to 100 nucleotides for the benefits sensitive, rapid and stable hybridization as taught by Bresser et al. (Column 9, lines 50-58). Brown et al. do not teach the probes are covalently attached to said surface of said substrate. Chetverin et al. teach a similar array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support and wherein said probes are covalently attached to said surface of said substrate (page 7, first full paragraph and Claim 1) wherein the covalent attachment simplifies amplification by permitting vigorous washing of the covalently bound hybrids for purification of the hybrids prior to amplification (page 16, first full paragraph). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the stably associated probes of Brown et al. with the covalently attached probes of Chetverin et al. for the expected benefit of simplified hybrid purification and subsequent amplification.

Regarding Claim 23, Brown et al. teach an array (i.e. a multi-cell substrate) comprising a pattern of probe oligonucleotide spots (i.e. cells of the multi-cell substrate) (Column 11, lines 52-67) wherein the density of spots on said array does not exceed about 400/cm$^2$ (Column 11, 62-67) wherein the probe spots are bound to the surface of a solid support, wherein each probe spot corresponds to a target nucleic acid and comprises a composition of probes wherein the probes are at least 50 nucleotides in length (Column 13, lines 21-25) wherein each of said

probes exhibits substantially the same high hybridization efficiency with its respective target and a low level of non-specific hybridization i.e. the probes of each spot bind specifically to their binding partners and therefor exhibit substantially the same high hybridization efficiency and low level of non-specific hybridization (Column 6, lines 64-67 and Column 13, lines 16-20) but they do not specifically teach the probes range in length from about 65 to 90 nucleotides. However, probes of about 65 to 90 nucleotides were well known in the art at the time the claimed invention was made a taught by Bresser et al. who specifically teach that probes ranging in length from about 65 to 90 nucleotides provide the most sensitive, rapid and stable hybrids (Column 9, lines 50-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of at least 50 nucleotides taught by Brown et al. with the teaching of Bresser et al. wherein the preferred probes are about 65 to 90 nucleotides for the benefits sensitive, rapid and stable hybridization as taught by Bresser et al. (Column 9, lines 50-58). Brown et al. do not teach the probes are covalently attached to said surface of said substrate. Chetverin et al. teach a similar array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support and wherein said probes are covalently attached to said surface of said substrate (page 7, first full paragraph and Claim 1) wherein the covalent attachment simplifies amplification by permitting vigorous washing of the covalently bound hybrids for subsequent amplification (page 16, first full paragraph). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the stably associated probes of Brown et al. with the covalently attached probes of Chetverin et al. for the expected benefit of simplified hybrid purification and subsequent manipulation.

**Response to Arguments**

8. Applicant argues that Chetverin does not make of the deficiency of Brown et al. because Brown et al. do not teach the claimed probe length ranges. The arguments is deemed moot in view of the withdrawn rejections and new grounds for rejection. Additionally, the argument is not found persuasive for the reasons stated above in ¶ 6.

9. Claims 8 & 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998) and Bresser et al. (U.S. Patent No. 5,707,801, issued 13 January 1998) and Chetverin et al. (WO 93/17126, 2 September 1993) as applied to Claim 7 above and further in view of Graves D. (TibTech, March 1999, 17: 127-134).

Regarding Claims 8 & 9, Brown et al. teach the array (i.e. a multi-cell substrate) comprising at least one pattern of probe oligonucleotide spots (i.e. cells of the multi-cell substrate) (Column 11, lines 52-67) wherein the probe spots are stably associated with the surface of a solid support (Column 4, lines 35-44), wherein each probe spot corresponds to a target nucleic acid and comprises a composition of probes wherein the probes are at least 50 nucleotides in length (Column 13, lines 21-25) but they do not specifically teach the probes range in length from about 65 to 90 nucleotides. However, probes of about 65 to 90 nucleotides were well known in the art at the time the claimed invention was made a taught by Bresser et al. who specifically teach that probes ranging in length from about 65 to 90 nucleotides provide the most sensitive, rapid and stable hybrids (Column 9, lines 50-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of at least 50 nucleotides taught by Brown et al. with the teaching of Bresser et al. wherein the preferred probes are about 65 to 90 nucleotides for the benefits sensitive, rapid and stable hybridization as taught by Bresser et al. (Column 9, lines 50-58). Brown et al. do not teach the probes are cross-linked to said surface of said substrate. Chetverin et al. teach a similar array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support and wherein said probes are covalently attached to said surface of said substrate (page 7, first full paragraph and Claim 1) wherein the covalent attachment simplifies amplification by permitting vigorous washing of the covalently bound hybrids for subsequent amplification (page 16, first full paragraph) but Chetverin et al. do not each the probes are cross-linked to the surface of said substrate at at

least one site (Claim 8) and at at least two sites (Claim 9). However, probes cross-linked to the surface of a support were known and practiced in the art at the time the claimed invention was made as taught by Graves. Specifically, Graves teaches long oligonucleotide probes cross-linked to a support to firmly anchor the probes at multiple sites (page 131, third full paragraph, lines 1-13). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe attachments of Brown et al. and Chetverin et al. with the cross-linked attachment of Graves for the expected benefit of firmly attaching long probes to the support at taught by Graves.

**Response to Arguments**

10. Applicant argues that Chetverin and Graves do not make of the deficiency of Brown et al. because Brown et al. do not teach the claimed probe length ranges. The arguments is deemed moot in view of the withdrawn rejections and new grounds for rejection. Additionally, the argument is not found persuasive for the reasons stated above in ¶ 6.

11. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998), Bresser et al. (U.S. Patent No. 5,707,801, issued 13 January 1998) and Stratagene (catalog, 1988).

Regarding Claim 35, Brown et al. teach the components of an array (i.e. a multi-cell substrate) comprising at least one pattern of probe oligonucleotide spots i.e. cells of the multi-cell substrate wherein each cell comprises a microarray (Column 11, lines 52-67) wherein the probe spots are stably associated with the surface of a solid support (Column 4, lines 35-44), wherein each probe spot corresponds to a target nucleic acid and comprises a composition of probes wherein the probes are at least 50 nucleotides in length (Column 13, lines 21-25) but they do not specifically teach the probes range in length from about 65 to 90 nucleotides. However, probes of about 65 to 90 nucleotides were well known in the art at the time the claimed invention was made a taught by Bresser et al. who specifically teach that probes ranging in length from about 65 to 90 nucleotides provide the most sensitive, rapid and stable hybrids (Column 9, lines 50-58). It would have been obvious to one of ordinary skill in the art

at the time the claimed invention was made to modify the probes of at least 50 nucleotides taught by Brown et al. with the teaching of Bresser et al. wherein the preferred probes are about 65 to 90 nucleotides for the benefits sensitive, rapid and stable hybridization as taught by Bresser et al. (Column 9, lines 50-58). Brown et al. and Bresser et al. do not teach the components of the array combined in to a kit. However, Stratagene catalog teaches a motivation to combine reagents into kit format (page 39). It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the array components of Brown et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

**NEW CLAIMS**

12. Claims 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998) and Bresser et al. (U.S. Patent No. 5,707,801, issued 13 January 1998) as applied to Claim 1 and 14 above.

Regarding Claims 36 and 37, Brown et al. teach an array (i.e. a multi-cell substrate) comprising a pattern of probe oligonucleotide spots (i.e. cells of the multi-cell substrate) (Column 11, lines 52-67) wherein the probe spots are bound to the surface of a solid support, wherein each probe spot corresponds to a target nucleic acid and comprises a composition of probes wherein the probe have a length of at least 50 nucleotides (Column 13, lines 21-25) but they do not specifically teach the probes range in length from about 50 to 120 nucleotides (Claim 36) and 60 to 100 nucleotides (Claim 37). However, probes of about 50 to 120 and 60 to 100 nucleotides were well known in the art at the time the claimed invention was made a

taught by Bresser et al. who specifically teach that probes ranging in length from about 50 to 120 nucleotides provide the most sensitive, rapid and stable hybrids (Column 9, lines 50-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of at least 50 nucleotides taught by Brown et al. with the teaching of Bresser et al. wherein the preferred probes are about 50 to 120 nucleotides or 60 to 120 for the benefits sensitive, rapid and stable hybridization as taught by Bresser et al. (Column 9, lines 50-58). Brown et al. do not specifically teach the variance in hybridization efficiency does not exceed about 10 fold however, they teach the probes of each spot bind specifically to their binding partners (Column 6, lines 25-28 and 47-58). Therefore one of skill in the art would have reasonably expected hybridization efficiency variance to not exceed 10-fold.

13. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998) and Bresser et al. (U.S. Patent No. 5,707,801, issued 13 January 1998) and Chetverin et al. (WO 93/17126, 2 September 1993). as applied to Claim 23 above.

Regarding Claim 38, Brown et al. teach an array (i.e. a multi-cell substrate) comprising a pattern of probe oligonucleotide spots (i.e. cells of the multi-cell substrate) (Column 11, lines 52-67) wherein the density of spots on said array does not exceed about 400/cm$^2$ (Column 11, 62-67) wherein the probe spots are bound to the surface of a solid support, wherein each probe spot corresponds to a target nucleic acid and comprises a composition of probes wherein the probes are at least 50 nucleotides in length (Column 13, lines 21-25) wherein each of said probes exhibits substantially the same high hybridization efficiency with its respective target and a low level of non-specific hybridization i.e. the probes of each spot bind specifically to their binding partners and therefor exhibit substantially the same high hybridization efficiency

and low level of non-specific hybridization (Column 6, lines 64-67 and Column 13, lines 16-20) but they do not specifically teach the probes range in length from about 65 to 90 nucleotides. However, probes of about 65 to 90 nucleotides were well known in the art at the time the claimed invention was made a taught by Bresser et al. who specifically teach that probes ranging in length from about 65 to 90 nucleotides provide the most sensitive, rapid and stable hybrids (Column 9, lines 50-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of at least 50 nucleotides taught by Brown et al. with the teaching of Bresser et al. wherein the preferred probes are about 65 to 90 nucleotides for the benefits sensitive, rapid and stable hybridization as taught by Bresser et al. (Column 9, lines 50-58). Brown et al. do not teach the probes are covalently attached to said surface of said substrate. Chetverin et al. teach a similar array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support and wherein said probes are covalently attached to said surface of said substrate (page 7, first full paragraph and Claim 1) wherein the covalent attachment simplifies amplification by permitting vigorous washing of the covalently bound hybrids for subsequent amplification (page 16, first full paragraph). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the stably associated probes of Brown et al. with the covalently attached probes of Chetverin et al. for the expected benefit of simplified hybrid purification and subsequent manipulation. Brown et al. do not specifically teach the variance in hybridization efficiency does not exceed about 10 fold. However, they teach the probes of each spot bind specifically to their binding partners (Column 6, lines 25-28 and 47-58). Therefore one of skill in the art would have reasonably expected hybridization efficiency variance to not exceed 10-fold.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

**Conclusion**

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
August 2, 2001